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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/982,172 | 10/19/2001 | Emil Israel Katz | 01/22283 | 7823 |

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EXAMINER

ZHOU, SHUBO

ART UNIT PAPER NUMBER

1631

DATE MAILED: 03/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/982,172

Applicant(s)

KATZ, EMIL ISRAEL

Examiner

Shubo "Joe" Zhou

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10/9/03, and 12/4/03.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-63 is/are pending in the application.
- 4a) Of the above claim(s) 1-42, 51 and 56-63 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 43-50 and 52-55 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 19 October 2001 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date <u>2/28/02, 12/4/03</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Amendments

Applicants' election of Group V (claims 43-50, 52-55) in the response filed 10/9/03 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Accordingly, claims 1-63 are currently pending, claims 43-50, 52-55 are under examination, and claims 1-42, 51, and 56-63 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the response filed 10/9/03.

Information Disclosure Statement

The Information Disclosure Statements filed 2/28/02 and 12/4/03 have been entered and considered. Initialed copies of the form PTO-1449 are enclosed with this action.

Specification

The specification is objected to because of the following:

The title of the invention is not descriptive. The elected invention is drawn to a method of quantifying peptides in a biological sample, however, the title is directed to peptides representative of polypeptides of interest and antibodies directed thereagainst and methods, systems, and kits for generating and utilizing each. A new title is required that is clearly indicative of the invention to which the elected claims are directed.

It is noted that there are three different drawings of figure 4. It appears that they represent different portions of one illustration. If this is the case, it is suggested that Fig. 4A, Fig.4B and Fig. 4C be used, and the Brief Description of the Drawings section of the specification be amended accordingly.

Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 43-50, and 52-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fledelius et al. (US 6,420,125 B1, date of patent: Jul. 16, 2002, filed: Aug. 21, 2000) in view of Werkmeister et al. (Biochem. J. 274:895-898, 1991).

The claims are drawn to a method of quantifying peptides of interest from a biological sample comprising contacting a proteolysed biological sample with at least one antibody and at least one peptide of a plurality of peptides generated according to information derived from computational analysis of the polypeptide of interest. It appears to be a competitive immunoassay.

Fledelius et al. disclose a method of detecting collagen fragments from biological samples of body fluids. The method comprises contacting the samples with an antibody specific for certain sequences of collagen and synthetic peptides that also bind to the antibody in a competitive immunoassay. See columns 7, 11 and 14. The method also comprises labeling the antibodies with a detectable marker such as enzymes, chromophores, fluorophores, chemiluminescent materials or radio-isotopes. See column 8. Fledelius et al. also disclose that the immunoassay itself can be conducted using any procedure selected from a variety of protocols known in the art. The immunological binding partner, i.e. the antibody, may be complexed to a solid support and used as a capture immunological binding partner for the analyte to be assayed, i.e. the collagen fragments. See columns 11 and 12. Such solid support with the antibodies attached thereon is interpreted as a microarray.

However, Fledelius et al. do not explicitly recite that the biological samples are proteolysed prior to binding to antibodies, and that the competitive synthetic peptides are generated based on computer analysis of the polypeptide of interest.

Werkmeister et al. disclose that 8 monoclonal antibodies highly specific for collage (type III) are generated with proteolytic fragments of collagen digested with pepsin, and that the antibodies are specific to several epitopes of collagen tested by allowing the antibodies to bind to

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fragments of collagen digested by different proteolytic reagents such as trypsin and CNBr. See Abstract and Experimental, page 895. Werkmeister et al. et al. further disclose that the epitopes are present throughout the entire length of the collagen, and that some epitopes can be recognized by some antibodies on a proteolytic fragment obtained by digestion with Trypsin but not with CNBr. See page 897. Werkmeister et al. also state that regions of greater chain flexibility may represent the major epitopes on a molecule, and that parameters such as conformational energy calculations, thermal stability of fragments and susceptibility of the collagen helix to proteolysis may allow reasonable estimate of the flexibility of a region.

A person of ordinary skill in the art would have been motivated by Werkmeister et al. to modify Fledelius et al. to use the 8 antibodies generated by Werkmeister et al. for the detection of collagen from body fluids due to the antibodies' high specificity to collagen. Since the antibodies are generated from proteolytic fragments of collagen, and since the epitopes recognized are present throughout the entire length of the collagen, one of ordinary skill in the art would have been motivated by Werkmeister et al. to modify the method of Fledelius et al. to proteolyse the biological samples prior to binding with a proteolytic agent such as trypsin or CNBr to assure that all epitopes of the collagen molecules are accessible to the antibodies. Further, one of ordinary skill in the art would have been motivated by Werkmeister et al. to generate the synthetic peptides used for competition in the competitive assay of Fledelius et al. corresponding to the proteolytic fragments of the samples to make sure that the synthetic peptides are the same as those proteolytic fragments in the sample for an ideal competition. To synthesize these proteolytic fragments, an analysis of the collagen sequence to identify the proteolytic sites, etc. would have been necessary and reasonably doable, and the analysis would

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have been a computational analysis because the sequence of collagen would have been large and available in a public computer database.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shubo (Joe) Zhou, whose telephone number is 571-272-0724. The examiner can normally be reached Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on 571-272-0722. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

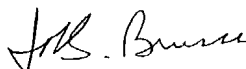
Any inquiry of a general nature or relating to the status of this application should be directed to Patent Analyst William Phillips whose telephone number is 571-272-0548, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Shubo (Joe) Zhou, Ph.D.



Patent Examiner

 18 March 2007
JOHN S. BRUSCA, PH.D.
PRIMARY EXAMINER